

### **Remarks**

In light of the following Remarks, reconsideration and allowance of the above-captioned application are respectfully requested.

The pending claims are directed to novel calix [4] pyrroles. More specifically, the presently pending claims are directed to particular meso-substituted calix [4] pyrroles that can be utilized to bind molecular species in solution and in the solid state in a highly effective and selective way.

In the Office Action, the reference in the previously submitted IDS to the Background section of the pending application was not considered, because it was not in conformance with MPEP 609. An Information Disclosure Statement is being submitted in conjunction with the current Request for Continued Examination. Along with certain recently discovered references, the submitted IDS individually lists the references discussed in the Background section of the application. At the present time, no legible copy of certain of the listed references is possessed or in control of the Applicants or their representatives. It is Applicants' understanding, however, that a concise explanation of the relevance of these documents, as it is presently understood by the Applicants, may be found in the discussion in the Background section of the application. By disclosure of any specific document to the Patent Office, Applicants do not admit that such document is effective as prior art against the above-identified application. Additionally, submission of any document is not to be taken as an admission of the materiality of the document to the prosecution of the present application.

In the Office Action, claims 30-33 were rejected under 35 U.S.C. §103(a) as being unpatentable over Gale, et al. (U.S. Patent No. 6,262,257). As pointed out in the Office Action, tetraspirocyclohexylcalix[4]pyrrole is disclosed in the patent as is the generic teaching of the coupling of two of the substituents listed in paragraphs i) and ii) of column 7 attached to the meso-carbon of a calix[4]pyrrole to form a bridged structure. The patent does not, however, disclose the synthesis of tetraspirocycloheptylcalix[4]pyrrole or tetraspirocyclooctylcalix[4]pyrrole, as is found in claims 30-33 of the present application. In the Office Action, it was suggested that it

would have been obvious to a person of ordinary skill in the art at the time of the invention was made to synthesize any size of ring.

To support a *prima facie* case of obviousness, there must be some suggestion or motivation to one of ordinary skill in the art to modify the reference in the suggested manner and there must be a reasonable expectation that the modification will be successful. The suggestion to make the modification and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In addition, a reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984).

Applicants respectfully submit that in the present case, a *prima facie* case of obviousness has not been established for at least the reason that the suggestion or motivation to one of ordinary skill in the art to modify the reference is not found when the reference is viewed in its entirety. Moreover, Applicants further submit that even were the modifications to be made absent the necessary motivation, there is not found in the reference a reasonable expectation that such a modification would be successful in producing the disclosed highly selective separation materials.

Gale, et al., teaches certain calix[4]pyrroles that can be utilized in the field of separation technology. In particular, the separation technology of Gale, et al. is based on noncovalent interactions to provide efficient and effective separation of difficult-to-separate anions and molecules (col.1, ll.18-29). In addition, the reference teaches that part of the difficulty in recognition and separation of compounds, and in particular neutral compounds, is that these molecules have few functionalized sites available for hydrogen bonding, and they lack the large hydrocarbon surfaces necessary to participate in efficient  $\pi$ - $\pi$  stacking. At column 5, beginning at line 20, the reference provides further description of the separation abilities of the disclosed materials. Specifically, the reference teaches that the affinity a macrocycle has for a particular species can be "tuned" by strategic choice of electron-donating or electron-withdrawing peripheral substituents for synthesis of the macrocycle.

At the paragraph beginning at column 16, line 3, an extensive listing of compositions of matter provided by the reference is given. In particular, the invention provides  $\beta$ -substitued calix[n]pyrroles, calix[m]pyridines, calix[n]pyrrole-anion complexes, calix[m]pyridino[n]pyrrole-anion complexes, calix[n]pyrrole-neutral molecule complexes, calix[m]pyridino[n]pyrrole-neutral molecule complex, calix[m]pyridino[n]pyrrole-cation complexes, calix[m]pyridine-cation complexes, calix[m]pyridine-neutral molecule complexes and certain meso-substituted calix[4]pyrroles, meso-substituted calix[n]pyrroles where n is 5, 6, 7, or 8, certain calix[m]pyridino[n]pyrroles, where  $m+n=4$ , and calix[m]pyridino[n]pyrroles where  $m+n=5, 6, 7$ , or 8 (emphasis added). As can be seen, the reference itself is directed to only certain meso-substituted calix[4]pyrroles, and thus, is not intended to encompass any and all meso-substituted calix[4]pyrroles.

Moreover, the reference goes on to describe further what particular calix[4]pyrroles are encompassed by the patent. For instance, beginning at column 23, the patent describes embodiments including calix[n]pyrroles having an ester functionality at a meso-carbon and those having an acid functionality at a meso-carbon. Also described are other possible calix[4]pyrroles in the paragraph at column 24, line 25. Additional meso-substituted calix[4]pyrroles encompassed by the invention are described in Example 2, with those being described having functional groups for further derivatization and including meso-monoesters, meso-monoacids, as well as other meso-groups including alkene groups, sulfurs, arenes, NH,  $\text{NH}_2^+$ ,  $\text{NHCH}_3^+$ ,  $\text{N}(\text{CH}_3)_2$ , NOH,  $\text{NNH}_2$ , and  $\text{NN}(\text{CH}_3)_2$  functionalities. All of these described additions or functionalizations on the basic disclosed octamethyl- or tetraspirocyclohexyl-calix[4]pyrrole skeletons are described as being suitable for utilization as what the patent terms as a 'hook' for use as a synthon for the production of derivatives.

In summation then, when taken in its entirety, the reference teaches certain calix[4]pyrrole materials that can be further functionalized for utilization in the production of derivatives. Notably, the described functionalizations are fairly reactive in nature. In addition, the patent teaches that the affinity of the disclosed substances for targeted molecules in separation techniques can be tuned by choice of electron-

donating or electron-withdrawing peripheral substituents. Moreover, the patent teaches that these separation techniques can rely on hydrogen bonding capabilities and  $\pi$ - $\pi$  stacking. Thus, when taken in its entirety, the reference may possibly suggest modification of the disclosed materials with the addition of reactive constituents to the basic calix[4]pyrrole skeletal structures, and in particular, the addition of reactive constituents that can provide  $\pi$ - $\pi$  stacking with a targeted molecule, but even this possibility is remote, as the patent states that only certain calix[4]pyrroles are encompassed in the invention.

Presently pending claims 30-33, in contrast, include a larger ring structure on the meso-substituted carbon. The larger ring structures of the tetraspirocycloheptyl—and the tetraspirocyclooctyl- calix[4]pyrroles of claims 30-33 do not add  $\pi$ - electrons to the materials. In addition, the larger ring structure does not materially increase the reactivity of the materials through addition of an electron withdrawing or electron donating group. In fact, the method for improvement in the selectivity of the materials of the pending claims, which is believed to be brought about due to the alteration in the geometric structure of the molecules (though the inventors do not wish to be bound by any particular theory), has not been found to be mentioned or discussed in Gale, et al. as a possible method for improving the patented materials. In contrast, when taken in its entirety, Gale, et al. would instead appear to suggest that the electrical structure of the materials is of primary importance in modifying the materials, and mere modification of the geometric structure, with no substantial alteration in the electrical nature of the materials brought about in conjunction with the geometric alteration, would not successfully improve the usefulness of the materials in separation techniques.

As such, Applicants respectfully maintain that when considered in its entirety, there is no suggestion or motivation found in Gale, et al. to increase the size of the meso-carbon ring structure to obtain the materials of claims 30-33. In addition, Applicants further maintain that there is no suggestion found in the reference that such a modification could be successful in providing materials displaying highly efficient and selective separation capabilities for targeted constituents from liquids or solids.

In the Office Action, claims 34-35 were rejected under 35 U.S.C. §103(a) as being unpatentable over Gale, et al. In particular, it was stated that the materials of claims 34 and 35 are rendered obvious by the disclosure by Gale, et al. of tetraspirocyclohexylcalix[4]pyrrole and that the materials are homologues of one another. Moreover, it was stated that homologues are expected to be preparable by the same method and to have generally the same properties and this expectation is deemed to be the motivation for preparing the claimed materials.

Applicants respectfully submit that no support for such expectations can be found, and thus, the required motivation for modifying the teachings of the reference to arrive at the claimed materials is not met. As a result, Applicants further submit that a *prima facie* case of obviousness has not been supported, and the pending claims patentably define over the cited reference.

As discussed above, there must be some suggestion or motivation to one of ordinary skill in the art to modify the reference in the suggested manner. In the Office Action, it was stated that as part of this necessary motivation for modifying the teachings of the cited reference to arrive at the claimed products, the materials are expected to be preparable by the same method. However, the methyl cyclohexyl derivative of the claimed tetraspiro (2-methyl cyclohexyl) calix (4) pyrrole is obtained, for instance, by using methyl cyclohexanone as a reactant, rather than cyclohexanone. Although these reactants differ structurally by only a methyl group, the difference in their chemical nature could result in a substantial difference in their reactivity with other reactants. Further, the ability to form tetraspiro (2-methyl cyclohexyl) calix (4) pyrrole also depends on other reaction parameters, such as the thermodynamic and kinetic reaction conditions, the involvement of steric factors, etc. These parameters affect the success of obtaining the desired product and may greatly differ based on the reactants chosen. Thus, the outcome of the reaction is unpredictable and certainly not reasonably expected from the teachings of Gale, et al. This lack of expectation becomes even more evident in light of the fact that the methods disclosed in the presently pending application for forming the claimed materials are different (and in fact, patentably distinct) from those utilized in forming the materials of Gale, et al.

Thus, Applicants maintain that there is no suggestion found that the claimed materials could be formed by the same methods as were used to form the materials disclosed by Gale, et al.

In addition, Applicants submit that there is no teaching found to suggest that the claimed materials and those of Gale, et al. would be expected to have the same properties. For instance, claims 34 and 35 are directed to materials that include the methyl group only in the 2-position of the cyclohexyl ring. This particular position has been found by the inventors to show the desired effect, wherein materials including the substituent methyl group having as an alternative location the C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, or C<sub>6</sub> location did not exhibit the desired effect and hence are not claimed in the invention. As is generally known in the art, properties of any particular compound can be significantly effected by any substitution to a basic skeleton. For example, materials such as those described in references submitted in the attached Information Disclosure Statement (in particular, XP-002056653 and GB 2023 594) have very similar skeletal structures, but impart very different activity upon substitution of an alkyl group. Thus, a particular substitution of a basic skeleton can not be assumed to provide a material having generally the same properties as the skeleton itself, as suggested in the Office Action. This assumption is particularly unfounded in light of the fact that the materials in question, meso-substituted calix[4]pyrroles, have been taught not only by the present Applicants, but also by the cited reference as being capable of being particularly 'tuned' through selection of substituents to display affinity for a target molecule (though, as discussed above, the Gale, et al. recognized and suggested only limited methods for 'tuning' the materials, in particular, through selection of electron-donating or electron-withdrawing peripheral substituents).

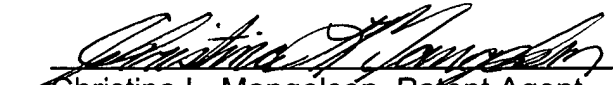
Therefore, for at least these reasons, Applicants respectfully submit neither the expectation to be preparable by the same method nor the expectation of having the same general properties can be found between the claimed materials and the tetraspirocyclohexylcalix[4]pyrrole of Gale, et al., and thus, proper motivation to support a *prima facie* case of obviousness has not been established and as a result, claims 34 and 35 patentably define over Gale, et al.

In the Office Action, claims 30-35 were objected to because claim 32 duplicates claim 30, claim 33 duplicates claim 32, and claim 35 duplicates claim 34. Applicants respectfully request that the Objection be withdrawn as the test as to whether a claim is a proper dependent claim is that it shall include every limitation of the claim from which it depends or, in other words, that it shall not conceivably be infringed by anything which would not also infringe the basic claim. A dependent claim does not lack compliance with 35 U.S.C. §112, fourth paragraph, simply because there is a question as to the significance of the further limitation added by the dependent claim or whether the further limitation in fact changes the scope of the dependent claim from that of the claim from which it depends.

Applicants believe that the present application is in complete condition for allowance and favorable action, therefore, is respectfully requested. The Examiner is invited and encouraged to telephone the undersigned, however, should any issues remain after consideration of this Request. Please charge any additional fees required by this Amendment to Deposit Account No. 04-1403.

Respectfully submitted,

12/22/04  
Date

  
Christina L. Mangelsen, Patent Agent  
Reg. No. 50,244

DORITY & MANNING, P.A.  
P.O. Box 1449  
Greenville, SC 29602  
(864) 271-1592  
(864) 233-7342